



January 10, 2011



Rear Admiral William S. Stokes
Director, National Toxicology Program Interagency Center
for the Evaluation of Alternative Toxicological Methods
National Institute of Environmental Health Sciences
P.O. Box 12233 Mail Code K2-16
Research Triangle Park, NC 27709

Dear Admiral Stokes,

I am responding to Dr. Linda Birnbaum's September 2, 2010 letter requesting NLM review of the recommendations for alternative testing methods and strategies to further reduce and refine the use of animals for assessing the ocular hazard potential of chemicals and products. The four ICCVAM Test Methods Evaluation Reports (TMERs) included in this request are:

- 1) **Recommendations for Routine Use of Topical Anesthetics, Systemic Analgesics, and Humane Endpoints to Avoid or Minimize Pain and Distress in Ocular Safety Testing.** (Recommends pain management procedures that should always be used to avoid or minimize pain and distress if the rabbit eye test is needed for regulatory safety purposes.)
- 2) **Current Validation Status of In Vitro Test Methods Proposed for Identifying Eye Injury Hazard Potential of Chemicals and Products.** (Recommends that the Cytosensor Microphysiometer (CM) test method can be used: a) as a screening test to identify some types of substances that may cause permanent or severe eye injuries, and b) to determine if some types of substances will not cause sufficient injury to require hazard labeling for eye irritation. Four other *in vitro* test methods were evaluated and it was concluded that improved predictivity is needed before they can be used for regulatory safety testing. Recommendations for future studies that could potentially improve these test methods are included.
- 3) **Current Validation Status of a Proposed In Vitro Testing Strategy for U.S. Environmental Protection Agency Ocular Hazard Classification and Labeling of Antimicrobial Cleaning Products.** (Recommends studies to characterize the usefulness and limitations of a non-animal *in vitro* testing strategy that uses three *in vitro* test methods.)
- 4) **Recommendation to Discontinue Use of the Low Volume Eye Test for Ocular Safety Testing.** (Recommends that a proposed low volume rabbit eye test should not be used for regulatory testing due to performance issues.)


NLM agrees with ICCVAM's recommendations about these alternative testing methods and strategies. The ICCVAM evaluation process included scientific peer review by an international independent panel or experts, review by the federally chartered Scientific Advisory Committee on Alternative Toxicological Methods (SACATM), and also included several public commenting opportunities. ICCVAM considered the peer review report, and the SACATM and public comments in preparing the final recommendations.

As you know, we do not have any regulatory or testing authority that would need to be in compliance with these recommendations. We continue to heartily endorse the recommendations and the continued work to promote and encourage the development and use of alternative test methods that are found to be effective and applicable. We will include access to this information via ALTBIB, our NLM Web portal on "Resources on Alternatives to the Use of Live Vertebrates in Biomedical Research and Testing" (<http://toxnet.nlm.nih.gov/altbib.html>).

We are pleased to continue to participate in the important efforts of the ICCVAM, and look forward to be on this committee as it works to facilitate the evaluation and adoption of test methods that provide improved animal welfare as while protecting human health and the environment.

Yours truly,

/s/

 Dr. Donald A.B. Lindberg
Director